

UNIVERSITY OF PENNSYLVANIA

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PANCREATIC JUICE

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A THESIS

IN PHYSIOLOGICAL CHEMISTRY

PRESENTED TO THE FACULTY OF THE GRADUATE SCHOOL IN

PARTIAL FULFILMENT OF THE REQUIREMENTS FOR

THE DEGREE OF DOCTOR OF PHILOSOPHY

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THE COMPOSITION OF PANCREATIC JUICE AND BLOOD SERUM AS INFLUENCED BY THE INJECTION OF ACID AND BASE.*

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INTRODUCTION.

The composition of the external secretions of various glands of the body is actively controlled by the glands themselves. These secretions, though composed of materials supplied by the same circulating blood serum, differ widely in their composition and reaction. We have, for example, nearly neutral saliva, acid gastric juice, alkaline bile and pancreatic juice; and we may add to this list urine of widely varying composition and reaction. This suggests (a) that the gland acts as a semipermeable membrane of unknown complexity and (b) that within the gland chemical reactions between diffusible substances and non-diffusible materials probably occur.

It was thought that some information might be obtained concerning the formation of a fluid secreted by a gland by studying the changes in the composition of the secreted fluid brought about by experimental variations in the composition of the blood serum during the period of secretion. In this paper data are presented to show the effect of intravenous injections of sodium carbonate and hydrochloric acid on the hydrogen ion, carbon dioxide, and chloride concentrations of both pancreatic juice and serum.

* This and the following paper constitute a thesis submitted to the Graduate School of the University of Pennsylvania in partial fulfillment of the requirements for the degree of Doctor of Philosophy. The investigation was carried out under the direction of Dr. D. Wright Wilson.

† Henry Strong Denison Medical Foundation Fellow, 1928-29.

Data on the changes in the concentrations of these same constituents in pancreatic juice with variations in glandular activity are also given.

The alkalinity of pancreatic juice as reported by previous workers varies over a wide range. Bayliss and Starling (1) reported pancreatic juice with an alkalinity equivalent to a 0.1 N sodium carbonate solution. Other workers, DeZilwa (2), Morel and Terroine (3), and Mellanby (4), found titratable alkalinities varying from 0.05 N to 0.16 N. pH values for pancreatic juice show as wide a variation: Foa, 9.79 to 10.21 (5); Auerbach and Pick, 7.3 to 8.7 (6); Archangelskii, 8.41 to 8.53 (7); Kestner and Plaut, 7.34 (8); Carnot and Gruzewska, 8.71 to 8.98 (9); Dubois and Polonovski, 7.8 to 8.7 (10); Still and Barlow, 7.85 to 8.30 (11). Czubalski (12) showed that the alkalinity of pancreatic juice varied with the rate of secretion, obtaining pH values ranging from 7.06 on slowly secreted juice to 8.64 on juice more rapidly secreted. Other workers report this same observation (Glaessner (13) and Wohlgemuth (14)). Some of these values were determined electrometrically, though none of the workers state definitely what precautions were used to prevent loss of free carbon dioxide while collecting the juice. More recently Gamble and McIver (15) have shown that the chloride and bicarbonate concentrations of pancreatic juice vary inversely and suggest that the alkalinity is thereby controlled.

Experimental Methods.

Large dogs (15 to 20 kilos) were used in order to obtain pancreatic ducts that could be easily cannulated and to insure a large flow of juice. An animal that had not been fed for the previous 24 hours was anesthetized by an intraperitoneal injection of amytal, a right rectus incision was made, and the duodenum and adjoining pancreas delivered into the wound, care being taken to handle the pancreas as little as possible. A glass cannula was then tied in the major pancreatic duct and at least one accessory duct ligated. In order to prevent kinking of the duct the cannula was held in position by suturing it to the intestine. Glass tubing was connected to the cannula by means of a short piece of rubber tubing. The duodenum was returned to the abdominal cavity and the incision closed around the glass tubing.

Since there was not a normal flow of juice immediately after the operation, secretin was injected into the jugular vein. The secretin was prepared by the method of Cowgill and Mendel (16), which was the most convenient and yielded the most active preparation of any method tried. Juice so obtained was clear and

colorless. After the juice had filled the glass tubing connected to the cannula, a tonometer filled with mercury was connected and the juice collected under a slight negative pressure. This procedure was found necessary when the hydrogen ion concentration was to be determined. Pancreatic juice is so poorly buffered that when collections are made under oil sufficient loss of free carbon dioxide occurs to cause appreciable pH changes. Some samples were collected under oil in graduated 15 cc. centrifuge tubes, to enable the rate of secretion to be determined. Samples collected in this manner are designated in the tables.

Since the rate of flow of pancreatic juice affects its alkalinity, the rate of secretion was kept as uniform as possible by injecting secretin at regular intervals, usually every 15 minutes. The first sample obtained was generally collected under oil, and considered to be a mixture of the preformed juice in the gland (capacity of ducts in the cat 1 to 1.5 cc. (17)), and the juice called forth by the secretin. A second sample, presumably true secretin juice, was then collected in a tonometer. An initial sample of blood was taken from the jugular vein, then an intravenous injection of a solution of acid or base was made followed by the drawing of a second blood sample. Two more samples of pancreatic juice were collected in tonometers and then a third blood sample was taken. Sometimes further collections were made. All blood samples were collected under oil, which was replaced by paraffin before centrifuging. The serum was drawn off into a tonometer. The animal was under anesthesia throughout the experiment and sacrificed at the end.

Analytical Methods.

Total carbon dioxide was determined on juice and serum by the method of Van Slyke and Stadie (18). Carbon dioxide tension of both fluids, reported as H_2CO_3 , was calculated from the total carbon dioxide and pH values by means of the following equation which is a combination of equations developed by Van Slyke.

$$\text{mm H}_2\text{CO}_3 = \frac{\text{mm total CO}_2}{10^{\text{pH} - \text{pK}'} + 1}$$

The value of 6.1 for pK' of serum, determined by Hastings, Sendroy, and Van Slyke (19) was used. Since the ionic activity of

pancreatic juice is probably similar to that of serum, it was assumed that this value for pK' could also be used for pancreatic juice. Bound carbon dioxide, reported as HCO_3 , was taken as the difference between total and free carbon dioxide. When no pH value was obtained, an average value of one mm of free carbonic acid was assumed for both serum and pancreatic juice, and bound carbon dioxide calculated accordingly. Since the free carbon dioxide is but a small fraction of the total, especially in the juice, any error in such calculation will cause but a negligible error in calculating the bound carbon dioxide concentration.

Chloride was determined by the method of Van Slyke as modified by Wilson and Ball (20).

Sodium was determined by the method of Kramer and Gittleman as modified by Kerr (21). Serum values were obtained on ashed samples, since direct determinations were found to yield unreliable results as reported by Kerr. Pancreatic juice was analyzed without ashing, since ashed and unashed samples gave identical results. Several samples of pancreatic juice, analyzed by both the micro and the macro chloroplatinate methods, gave checks within the experimental error.

The hydrogen ion concentrations of serum and of pancreatic juice were determined by means of the quinhydrone electrode¹ and colorimetrically at 38°. All samples were run within 6 hours of collection; no significant change in pH occurs in tonometer samples that have been allowed to stand this long. The quinhydrone method was shown to yield results, with dog serum, that agreed favorably with the hydrogen electrode determinations. Samples of pancreatic juice collected in tonometers run by both methods gave pH values with the quinhydrone electrode of (1) 8.16 and (2) 7.93, and with the hydrogen electrode of (1) 8.14 and (2) 7.92. Colorimetric determinations on both fluids were run by the Hastings and Sendroy (22) modification of the Cullen method. Colorimetric and quinhydrone pH values for pancreatic juice agreed within experimental errors. The two methods showed variations with serum of a magnitude similar to those reported by Johnston (23) for the hydrogen electrode and the colorimetric methods. pH values reported here are quinhydrone determinations unless otherwise stated.

¹ I wish to thank Mr. E. P. Laug for making these determinations.

Results.

Table I shows the influence of secretion rate on the juice composition. The more rapidly a juice was secreted the higher were the pH value and bound carbon dioxide concentration and the lower the chloride. Thus the concentrations of chloride and bicarbonate varied inversely, their sum being more or less constant regardless of the rate of secretion. A slowly secreted juice had a

TABLE I.
Influence of Secretion Rate on Juice Composition.

Dog No.	Juice No.*	Secretion rate. <i>cc. per min.</i>	mm per liter.			$\frac{\text{HCO}_3}{\text{Cl}}$	pH†
			HCO ₃	Cl	HCO ₃ + Cl		
27	2	0.29	93	47	140	2.0	8.12
	A	0.04	34	108	142	0.3	7.65
26	4 A	0.65	134	26	160	5.1	8.15
	5 A	0.12	86	66	152	1.3	8.05
23	2	0.19	120	36	156	3.3	
	3	0.03	56	79	135	0.7	
21	2	0.34	116	38	154	3.0	
	3	0.05	63	84	147	0.8	
20	2	0.42	126				
	1	0.01	46				

* All collected under oil.

† Colorimetric.

ratio of the concentrations of bicarbonate to chloride approaching that found in blood serum, namely 0.2, while in a rapidly secreted juice the magnitudes of the concentrations were reversed and a ratio of 3.3 obtained. This effect of secretion rate on juice composition was most noticeable when there was a large variation in the rate. Juices secreted rapidly but varying as much as 50 per cent in rate did not seem to show appreciable variations in composition.

In Tables II and III are recorded the effects of the intravenous injection of 0.5 N HCl in 0.9 per cent saline solution on the com-

position of blood serum and pancreatic juice. Acid injections were made very slowly and were accompanied by marked hyperpnea; no effect on the flow of pancreatic juice was observed.

Table II shows the results of an experiment in which the injection of acid caused a fall of 0.1 of a pH unit in the blood serum,

TABLE II.

Injection of Hydrochloric Acid.

Dog 29, weight 17.6 kilos.

Sample.	Time.	Amount.	Rate.	pH	mm per liter.			
					H ₂ CO ₃	HCO ₃	Cl	HCO ₃ + Cl
		cc.	cc. per min.					
Juice 1.*	10.35- 10.40 a.m.	2.7	0.54			102	47	149
" 2.	10.40- 11.15 a.m.	14	0.40	8.14	1.2	132	24	156
Serum 1.	11.15 "	40†		7.22	1.6	23	113	136
Injection.	11.33 "- 12.50 p.m.	72		0.5 N HCl in 0.9 per cent NaCl intravenously.				
Serum 2.	12.57 "	30†		7.12	1.6	16	119	135
Juice 3.	12.52- 1.25 p.m.	12	0.36	8.17	1.0	122	31	153
" 4.	1.30- 2.00 p.m.	20	0.66	8.18	1.0	121	30	151
Serum 3.	1.58 "	40†		7.11	1.7	16	118	134
Hemorrhage.	2.00 "	200†						
Juice 5.*	2.00- 2.30 p.m.	12.5	0.42			120	33	153

* Collected under oil.

† Amount of whole blood.

while the pancreatic juice showed a slight indication of an alkaline swing due mainly to a decrease in CO₂ tension. The bicarbonate and chloride contents of serum and pancreatic juice fell or rose an equivalent amount. The free CO₂ concentration of the blood serum was higher than that of the juice from the active gland. A light hemorrhage caused no change in the response of the gland to secretin or in the composition of the juice.

It will be observed that the initial blood serum is more acid

than normal. This has been found to be the case in all the dogs in this series of experiments, the quinhydrone results being con-

TABLE III.
Injection of Hydrochloric Acid.

Dog 26, weight 22.9 kilos.

Sample.	Time.	Amount.	Rate.	pH	mm per liter.			
					H ₂ CO ₃	HCO ₃	Cl	HCO ₃ + Cl
		cc.	cc. per min.					
Juice 1 A.*	10.52-	11.5	1.15			134	25	159
	11.02 a.m.							
" 1 B.*	10.52-	5.6	0.35			125	30	155
	11.08 a.m.							
Serum 1.	11.15 "	40†		7.22	1.7	23	110	133
Juice 2 A.	11.03-	18	0.49	8.12	1.3	137	21	158
	11.40 a.m.							
" 2 B.*	11.08-	7.2	0.26	8.12	1.3	133	22	155
	11.35 a.m.							
Injection.	11.45 " -	50			0.5 N HCl in 0.9 per cent NaCl intravenously.			
	12.28 p.m.							
Serum 2.	12.34 "	50†		7.31	1.2	20	114	134
Juice 3 A.	12.30-	18	0.72	8.14	1.2	129	29	158
	12.55 p.m.							
" 3 B.*	12.30-	7	0.25	8.14	1.2	135	31	166
	12.58 p.m.							
" 4 A.*	12.55-	13	0.65	8.10	1.3	134	26	160
	1.15 p.m.							
Serum 3.	1.10 "	40†		7.22	1.6	20	113	133
Juice 4 B.*	12.58-	8.5	0.26			137	27	164
	1.30 p.m.							
" 5 A.*	1.15-	5.4	0.12			86	66	152
	2.00 p.m.							
Hemorrhage.	6.15 "	500†						
Juice 6 A.*	6.15-	7.4	0.41			103	53	156
	6.33 p.m.							
Serum 4.	6.30 "	40†				19	112	131

* Collected under oil.

† Amount of whole blood.

firmed by hydrogen electrode determinations. The cause of this acid condition was not investigated. A contributing factor may have been the use of amytal, as a marked decrease in respiratory

rate can be observed when the anesthetic has taken effect. However, Hines, Boyd, and Leese (24) have reported that amytal does not affect the pH of blood serum.

The results given in Table III were obtained on a dog in which two ducts from different parts of the pancreas were cannulated. Juices from these were labeled A and B. Only slight differences in the composition of the juices were noted. The acid injection

TABLE IV.
Injection of Sodium Carbonate.

Dog 32, weight 12.4 kilos.

Sample.	Time.	Amount.	Rate.	pH	mm per liter.				
					H ₂ CO ₃	HCO ₃	Cl	HCO ₃ + Cl	Na
Juice 1.*	9.01– 9.14 a.m.	3.8	0.29			100	49	149	
“ 2.	9.14– 9.50 a.m.	10	0.28	8.13	1.1	120	33	153	157
Serum 1.	10.10 “	35†		7.27	1.4	20	110	130	133
Injection.	10.30– 11.55 a.m.	100		10 per cent Na ₂ CO ₃ intra- venously.					
Serum 2.	11.35 “	40†		7.38	1.7	33	105	138	154
Juice 3.	11.30 “ – 12.15 p.m.	12	0.27	8.15	1.2	135	33	168	181
“ 4.	12.15– 1.05 p.m.	16	0.32	8.24	1.0	133	37	170	181
Serum 3.	12.55 “	40†		7.36	1.8	33	108	141	155

* Collected under oil.

† Amount of whole blood.

in this experiment had little effect on the bound carbon dioxide and the serum actually became alkaline probably due to over-ventilation. The composition of the pancreatic juice showed little significant change throughout the experiment. Hemorrhage again produced no noticeable effects.

In Tables IV, V, and VI are tabulated the effects of the intra-venous injection of a 10 per cent sodium carbonate solution on the

composition of serum and pancreatic juice. No effect on the flow of juice was observed. In the experiment recorded in Table IV the injection of sodium carbonate caused the serum to become 0.1 pH more alkaline while the pancreatic juice showed a delayed rise of the same magnitude. The bicarbonate concentration of serum and pancreatic juice increased similarly after the injection, chloride values remaining more or less unchanged. Juice and

TABLE V.
Injection of Sodium Carbonate.

Dog 28, weight 17.6 kilos.

Sample.	Time.	Amount.	Rate.	pH	mm per liter.				
					H ₂ CO ₃	HCO ₃	Cl	HCO ₃ + Cl	Na
		cc.	cc. per min.						
Juice 1.	10.12– 10.47 a.m.	10	0.29	8.03	1.5	122	33	155	158
Serum 1.	10.21 “	40†		7.17	2.0	24	106	130	141
Injection.	10.52 “ – 12.08 p.m.	95		10 per cent Na ₂ CO ₃ intra- venously.					
Serum 2.	12.11 “	40†		7.45	1.9	41	106	147	154
Juice 2.	12.08– 12.38 p.m.	16	0.53	8.01	1.7	138	34	172	175
“ 3.	12.38– 1.10 p.m.	16	0.50	8.09	1.3	128	37	165	174
Serum 3.	1.13 “	40†		7.36	1.8	33	108	141	151
Juice 4.*	1.10– 1.45 p.m.	12.5	0.36	8.08	1.3	120	47	167	173

* Collected under oil.

† Amount of whole blood.

serum carbon dioxide tensions increased, the latter markedly, after the injection. The increase in sodium concentration of the serum was reflected quantitatively in the juice. This will be discussed in another paper.

Table V shows the sodium carbonate to have caused an alkaline swing of nearly 0.3 of a pH unit in the serum while a delayed rise of only 0.06 of a pH unit occurred in the juice. Values for bi-

carbonate and chloride concentrations were similar to those in Table IV. Serum carbon dioxide tension was lowered after injection while that of the pancreatic juice again increased.

TABLE VI.

Injection of Sodium Carbonate.

Dog 27, weight 12.1 kilos.

Sample.	Time.	Amount.	Rate.	pH	mm per liter.				
					H ₂ CO ₃	HCO ₃	Cl	HCO ₃ + Cl	Na
		cc.	cc. per min.						
Juice 1.*	8.17– 8.35 a.m.	5.6	0.31			95	51	146	
Serum 1.	8.33 “	40†		7.27	1.4	20	107	127	135
Juice 2.	8.35– 9.10 a.m.	10	0.29	8.20	0.8	93	47	140	149
Injection.	10.11– 10.40 a.m.	12			10 per cent Na ₂ CO ₃ intra-venously.				
Serum 2.	10.43 “	40†		7.35	1.3	23	106	129	
Juice 3.	10.42– 11.12 a.m.	10	0.33	8.20	0.8	102	48	150	151
“ 4.*	11.12– 11.43 a.m.	5.5	0.18	8.19	0.8	101	46	147	
“ 5.*	11.47 “ – 12.15 p.m.	4.2	0.13	8.10	1.0	96	51	147	
Hemorrhage.	12.27 “	230†							
Injection.	12.29– 12.43 p.m.	23			10 per cent Na ₂ CO ₃ intra-venously.				
Juice 6.*	12.44– 1.15 p.m.	4.8	0.15	8.02	1.0	85	68	153	159
Injection.	1.00– 1.11 p.m.	35			10 per cent Na ₂ CO ₃ intra-venously.				
Serum 4.	1.23 “	40†		7.59	1.1	34	103	137	153
Juice 7.	1.16– 1.55 p.m.	7.3	0.19	8.02	1.3	109	49	158	171

* Collected under oil.

† Amount of whole blood.

The results given in Table VI are those of a longer experiment. Three injections of sodium carbonate were made causing the pH and the bicarbonate concentration of the serum to increase.

The pancreatic juice also showed at first a similar increase of bicarbonate content with no change in pH. In later juices decreased pH values and bicarbonate concentrations with increased carbon dioxide tensions appeared in spite of the alkaline swing of the serum. It is possible that this was partly the result of a change in rate of flow.

It would seem that the main factor controlling the alkalinity of pancreatic juice is the rate of flow. The more rapid the rate of secretion, the higher the alkalinity of the juice. Intravenous injection of acid causing a lowered bicarbonate concentration of the serum and an acid swing, had little effect on pH values of pancreatic juice, though the bicarbonate content fell in an amount similar to that of the serum. Intravenous injections of sodium carbonate, causing an increased bicarbonate concentration and an alkaline pH swing of the serum, had a similar though less effect on the composition of pancreatic juice. The bicarbonate content increased immediately and in amount similar to that of the serum; pH values showed a delayed rise of smaller magnitude due mainly to the independence of the serum and pancreatic juice carbon dioxide tensions.

In other experiments in which acid salts (NaH_2PO_4) and lactic acid were injected, no significant pH changes in the serum or pancreatic juice were observed and the data are not reported; the injection of the lactic acid caused marked hemolysis.

DISCUSSION.

Though previous workers have claimed that pancreatic juice contains carbonate, values for bound carbon dioxide reported here are expressed as bicarbonate. Justification for this is seen if the ratio of carbonate to bicarbonate in a solution is calculated at a pH of 8.24, the highest value obtained in these experiments. Using the value of 10.22 for pK_2' of carbonic acid given by Michaelis (25):

$$\begin{aligned}\text{Log } \frac{\text{salt}}{\text{acid}} &= \text{pH} - \text{pK}_2' \\ &= 8.24 - 10.22 \\ \frac{\text{Salt}}{\text{Acid}} &= \frac{1}{100}\end{aligned}$$

In a juice with a pH of 8.24 about 1 per cent of the bound carbon dioxide is present as carbonate.

Since the juice bicarbonate is remarkably independent of the serum bicarbonate, it would seem that the serum is not the direct source of the juice bicarbonate. Hammarsten and Jorpes (26) have recently reported that prolonged secretion of pancreatic juice does not affect the alkaline reserve of the blood but does cause an acid swing in extracts made of the gland itself. They believe their results show that the sodium bicarbonate of the juice is formed by the action of the carbonic acid produced by the active gland on the alkali compounds, possibly salts of nucleic acids, of the pancreatic cells. The hydrogen ion is retained by the non-diffusible compounds and the sodium bicarbonate passes into the juice. The data presented in the present paper show that the alkalinity of the pancreatic juice increases with increased glandular activity, and that the carbon dioxide tension of the juice from the active gland is usually lower than the venous blood of the animal. These results would seem to support Hammarsten and Jorpes' conclusion that the carbon dioxide produced by the working gland is used to form a large part of the bound carbon dioxide of the juice it produces. However, it would seem from experiments reported in the following paper that the blood serum is the immediate source of the bases of the juice rather than alkali compounds of the gland itself. At any rate the pancreas appears to function so as to permit the free passage of base and the retention of hydrogen ions; the concentration of chloride and bicarbonate, and hence the alkalinity of the juice, varying with the gland's activity. This suggests the contrasting action of the stomach which appears to permit the free passage of chloride, and varies the concentration of hydrogen ion and base with changes in gland activity (McCann (27)).

On the other hand, Woinar (28) drew the conclusion that the total carbon dioxide content of pancreatic juice depends on the alkaline reserve of the blood serum and *vice versa*. He reported that continuous secretion of pancreatic juice causes a fall in serum alkaline reserve and a marked decrease in juice alkalinity which is, however, accompanied by a decreased rate of flow. Intravenous injection of sodium carbonate after prolonged secretion raises the juice alkalinity to above its original value as well as its rate of secretion. If the serum alkaline reserve is artificially lowered by

intravenous injections of acid, the bicarbonate concentration of the juice decreases as much as 50 per cent, the rate of flow also decreasing markedly. The data in the present paper indicate that Woinar probably failed to realize the importance of the rate of flow in influencing juice composition and for this reason was led to draw the erroneous conclusion that compositions of juice and serum run parallel.

Since the free carbon dioxide content of pancreatic juice is relatively constant and the rate of flow determines its bound carbon dioxide concentration and hence its alkalinity, it is of interest to inquire what the highest possible alkalinity of pancreatic juice is likely to be. The maximum rate of secretion obtained in these experiments is about 60 cc. per hour. This value compares favorably with the maxima obtained on dogs by other workers. Pawlow (29) reports values of 70 to 80 cc. an hour for large dogs. Elman and McCaughan (30) obtained a maximum of 500 cc. daily. This would seem to indicate that with the rapid rate of flow, pH values reported here are probably nearly maximal. However, it might be possible with a more rapid flow that all the inorganic cations would exist as bicarbonate ions. Since pancreatic juice is in osmotic balance with serum, as will be shown in the following paper, an inorganic cation concentration much greater than 150 mm is impossible in the normal animal. It might be argued that a very active gland would secrete carbonate instead of bicarbonate. If this occurred the total carbon dioxide content of the juice would be halved, for the constant amount of base in the juice could bind only half as much carbon dioxide in the form of carbonate as it would in the form of bicarbonate. In view of the fact that the bound carbon dioxide always increases as the rate of flow increases, there seems to be no tendency for carbonate to replace bicarbonate.

To calculate the maximum pH possible, we may assume a constant free carbon dioxide concentration of 1 millimol and a maximum bicarbonate of 150 millimols per liter.

$$\begin{aligned}\text{pH} &= \text{pK}' + \log \frac{\text{salt}}{\text{acid}} \\ &= 6.14 + \log \frac{150}{1} \\ &= 8.32\end{aligned}$$

If these assumptions are correct, the most alkaline juice obtainable has a pH of about 8.3. It would seem that values more alkaline than this, as reported by some workers, are due to loss of free carbon dioxide during collection. Since pancreatic juice is poorly buffered, the escape of free carbon dioxide may cause a marked alkaline swing. Even when juice is collected under oil, increase in alkalinity on standing is noticeable. For example, one sample collected under oil when first analyzed gave a pH of 8.10; after standing 3 hours a value of 8.16 was obtained.

On the other hand, juices secreted very slowly may have low pH values. Values similar to those of blood serum will be reported in permanent fistula dogs by Johnston and Ball (31). These juices have bicarbonate and chloride concentrations similar to blood serum.

It is of interest to compare the results obtained by other workers in similar experiments but on different body fluids. Carnot and Gruzewska (32) found that intravenous injections of sodium bicarbonate caused bile to become much more alkaline, the bicarbonate concentration of the bile increasing considerably. Gesell (33) showed that intravenous injections of sodium bicarbonate increased the alkalinity of lymph and blood about equally. Gesell and Hertzman (34) reported that sodium carbonate intravenously injected causes an increased alkalinity of cerebrospinal fluid while injections of sodium bicarbonate caused an acid swing in the fluid. They claim this difference in action of the two salts is due to the non-permeability of the base. Though bicarbonate injections were not made in the present study of pancreatic juice, it is not likely that a case analogous to cerebrospinal fluid would be found since the pancreatic cell seems to be freely permeable to sodium. Hug and Marenzi (35) found that intravenous injection of acid caused bile to become more alkaline, the bicarbonate content increasing. In a similar study on saliva, a slight increase in alkalinity was noted but a decrease occurred in the bicarbonate content. These results are similar to the effects of acid injection on the composition of pancreatic juice.

SUMMARY.

1. A study of the alkalinity of pancreatic juice and its relation to serum composition has been made.

2. The pH of the juice varies with its rate of flow. Juices secreted rapidly are the more alkaline, containing large amounts of bicarbonate and small amounts of chloride. In slowly secreted juices a lower alkalinity is found with large concentrations of chloride and small concentrations of bicarbonate. The sum of the bicarbonate and chloride concentrations is nearly constant regardless of the rate of flow.

3. Intravenous injections of hydrochloric acid cause but little change in the pH of pancreatic juice, regardless of the effect on the serum. Lowered bicarbonate values for serum are manifested quantitatively though not proportionally in the juice.

4. Intravenous injections of sodium carbonate solution, causing an alkaline swing in the serum, produce remarkably little change in the reaction of the juice. However, the increased concentration of bicarbonate and sodium in the serum appears quantitatively in the juice.

5. The possible significance of these findings and their relation to other studies of a similar nature is discussed.

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THE COMPOSITION OF PANCREATIC JUICE AND BLOOD SERUM AS INFLUENCED BY THE INJECTION OF INORGANIC SALTS.

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INTRODUCTION.

In the previous paper it was suggested that information concerning the permeability of the pancreatic tissue to the constituents of the blood serum could best be studied by determining the composition of pancreatic juice and serum during experimental variation in the composition of the latter. In that paper experiments were reported, in which acid and alkaline solutions were injected intravenously and the effect on the composition of the two fluids noted. It was found that the pH of pancreatic juice was practically not influenced by changes in the pH of the blood.

In this paper it is proposed to report further studies on the permeability of the pancreatic tissue to other ions common to both fluids. Solutions of salts containing one or more of the following ions: sodium, potassium, calcium, magnesium, chloride, and phosphate were injected into the blood stream and the composition of the serum and pancreatic juice before and after injection was determined.

Methods.

Experimental procedures for the collection of the pancreatic juice and serum were the same as described in the previous paper except that all samples were collected under oil. All solutions of salts were injected intravenously (jugular) except potassium chloride, which was injected intraarterially (femoral) to lessen its toxic effect.

The sodium, chloride, and bicarbonate concentrations of juice and serum were determined by the same methods described in the previous paper. The inorganic phosphate of both fluids was determined by the method of Fiske and Subbarow (1). The low concentration of phosphate in pancreatic juice made it necessary to add a certain known amount of phosphate before developing the color.

Potassium was determined on ashed samples of pancreatic juice and serum by the method of Kramer and Tisdall as modified by Kerr (2). Unreliable results were obtained on unashed samples of juice and serum, confirming Kerr's findings for serum. Several samples of pancreatic juice run by this method and the macro chloroplatinate procedure gave results that agreed within 5 per cent.

Calcium was determined by the method of Clark and Collip (3) on unashed samples of serum and juice. Ashed and unashed samples of pancreatic juice gave identical results.

Magnesium was determined by the method outlined by Briggs (4) with slight modifications. The addition of the potassium acid phosphate reagent to the filtrate from the calcium determination of pancreatic juice caused a fine precipitate of protein to form. Addition of the concentrated ammonia reagent had no effect on this precipitate. However it was found that if the order of addition of these two reagents was reversed, the ammonia being added first, then no precipitate occurred upon addition of the potassium acid phosphate. The order of addition of these reagents to the serum filtrate was immaterial. The amount of phosphate in the precipitate obtained was determined by the method of Fiske and Subbarow. Since the concentration of magnesium in the juice is small, standard phosphate solution must be added to the sample in order to give a color depth near that of the standard.

Total nitrogen of pancreatic juice was determined by the micro-Kjeldahl method of Folin and Denis (5). Total solids were determined by drying a measured sample at 105–110° overnight in a platinum crucible and weighing the residue. Freezing points were determined on a few samples of juice and serum by means of the apparatus devised by Stadie and Sunderman¹ (6). Qualitative

¹ I wish to thank Dr. F. W. Sunderman for making these determinations.

tests for sulfates were carried out on samples of juice with negative results.

Results.

In Table I are presented data on the composition of serum and pancreatic juice before and after the intravenous injection of a 10 per cent solution of sodium chloride. The injection had no noticeable effect upon the rate of secretion of the juice. Freezing points of both fluids determined before the injection showed that pancreatic juice and serum have osmotic pressures that are identical. The injection of sodium chloride caused a lowering in the freezing point of both serum and pancreatic juice of about the same magnitude. The fact that Juice 4 did not have a freezing point intermediate between that of Serums 2 and 3, as might be expected, was probably due to the unavoidable lag between the time of secretion of the juice and its collection, caused by the dead space between the secreting cells and the collecting tube. An indication of this lag was also shown by the sodium analysis, for in the first juice collected after the injection the sodium concentration increased 8 millimols, an amount identical to the increase in the serum collected immediately after the injection. The concentrations of potassium in the juice and serum were similar throughout, being unaffected by the injection. It will be noticed that the sums of the principle anion and cation concentrations expressed as mm per liter are somewhat higher in the juice than they are in the corresponding sera. However, if concentrations are expressed as mm per kilo of water, the inorganic compositions of the two fluids are more nearly identical. These relations were found to exist in all experiments and will be discussed in considering the compilation shown in Table VII. The concentrations of bicarbonate and chloride in the juice and serum varied inversely, as was shown in the preceding paper, depending on the rate of secretion of the juice.

Since the total concentration of inorganic salts of pancreatic juice is fairly constant (about 0.9 gm. of ash per 100 cc.), variations in total solids are mainly the result of variations in organic matter, probably protein. Continuous secretion appeared to deplete the gland of its organic materials as shown by the decrease in total solids from Juice 1 to 2. In the period during which Juice 3 was being

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slowly secreted, the gland appears to have partly replenished its store of organic matter as shown by the increase of solids in Juice 4, only a small part of which was due to the increased concentration of inorganic salts caused by the injection. In the following juices

TABLE I.
Injection of Sodium Chloride.

Dog 21, weight 16.2 kilos.

Sample.	Time.	Amount.	Δ	Total solids.	N	mm per liter.						mm per kilo water.	
						Na	K	HCO ₃	Cl	Na + K	HCO ₃ + Cl	Na + K	HCO ₃ + Cl
		cc.		gm. per 100 cc.	gm. per 100 cc.								
Juice 1.	10.38–	12		2.15	0.20	151	4.6	113	35	156	148	159	151
	11.11 a.m.												
Serum 1.	10.56 “	40*	0.561			143	3.3	25		146		159	
Juice 2.	11.32 “	14.2	0.558	1.74	0.14	151	4.1	117	38	155	155	158	158
	12.14 p.m.												
“ 3.	12.14–	2.5			0.20			64	84		148		151
	1.07 p.m.												
Injection.	12.48–	64	Injection of NaCl, 10 per cent intra-venously.										
	1.05 p.m.												
Serum 2.	1.09 “	40*	0.600			151	4.0	23	128	155	151	168	164
Juice 4.	1.07–	12.8	0.603	2.33	0.23	159	4.1	130	59	163	189	166	193
	1.27 p.m.												
Serum 3.	1.28 “	35*	0.582			145	4.3	21	124	149	145	162	158
Juice 5.	1.27–	4.0		1.71	0.12		4.4	125	40		165		168
	1.50 p.m.												
“ 6.	4.32–	9.5		1.63	0.11	164	5.1	101	61	169	162	172	165
	5.35 p.m.												
Serum 4.	5.27 “	40*				150	5.3	21	124	155	145	168	158

* Amount of whole blood.

another fall in total solids occurred with continuous secretion. The nitrogen of the juice showed the same variation as the total solids. If the total organic matter is computed by subtracting the total ash from the total solids, the total nitrogen is usually found to be about 16 per cent of the organic matter, as might be

expected if the organic material were protein. However in some juices the nitrogen varied from 11 to 28 per cent of the organic matter.

TABLE II.

Injection of Sodium Chloride.

Dog 19, weight 15.8 kilos.

Sample.	Time.	Amount.	Total solids.	N	mm per liter.					
					Na	K	HCO ₃	Cl	Na + K	HCO ₃ + Cl
		cc.	gm. per 100 cc.	gm. per 100 cc.						
Juice 1.	11.03-	13.7	3.79	0.44	157	4.1	104	54	161	158
	11.21 a.m.									
" 2.	11.21-	13.3	2.24	0.25	157	3.6	107	50	161	157
	11.47 a.m.									
Serum 1.	11.30 "	20*			138		23	112		135
Juice 3.	11.47 "-	10	1.74	0.10	155	3.5	104	57	159	161
	12.18 p.m.									
Injection.	12.18-†	57	Injection of NaCl, 10 per cent intravenously.							
	12.50 p.m.									
Serum 2.	12.26 "	10*			148			123		
Juice 4.	12.29-	8.5	2.64	0.24	170	2.9	113	56	173	169
	12.40 p.m.									
" 5.	12.40-	6.8	2.00	0.13	178	4.2	115	55	182	170
	12.50 p.m.									
Serum 3.	12.54 "	25*			148		23	128		151
Juice 6.	12.50-	11	1.75	0.13	176	3.8	112	58	180	170
	1.12 p.m.									
" 7.	1.12-	3.5		0.18	159		58	104		162
	2.37 p.m.									
" 8.	2.37-	12.9	2.33	0.22	175	4.2	114	53	179	167
	3.06 p.m.									
Serum 4.	3.12 "	25*			149	5.4	25	121	154	146

* Amount of whole blood.

† 32 cc. in at 12.24 p.m., injection then continued at rate of 1 cc. per min. until 12.50 p.m.

In Table II are presented the results obtained in another experiment where sodium chloride was injected. Here the injection was continued at a slower rate during the collection of Juices 4 and 5.

The results are similar to those obtained in the previous experiment. The increase in chloride concentration of the serum was accompanied not by an increase in chloride concentration of the juice, but by an increase in bicarbonate. Total solids of the juice showed an even more pronounced variation that again seems to depend on the previous state of activity of the gland. In the previous paper where injections of sodium carbonate were made, the

TABLE III.
Injection of Potassium Chloride.

Dog 23, weight 17.1 kilos.

Sample.	Time.	Amount.	Total solids.	mm per liter.					
				K	Na	Cl	HCO ₃	Na + K	Cl + HCO ₃
		cc.	gm. per 100 cc.						
Juice 1.	11.16-	5.6		6.0	152	36	121	158	157
	11.46 a.m.								
" 2.	3.51 p.m.-	8.4	1.92	6.1	152	53	105	158	158
	4.40 p.m.								
Serum 1.	4.15 "	20*		5.2	142	111	22	147	133
Injection.	4.49-	20							
	5.02 p.m.								
Serum 2.	5.06 "	20*		6.2	141	112	19	147	131
Juice 3.	5.03-	7.7	1.94	7.8	151	68	88	159	156
	5.36 p.m.								
" 4.	5.36-	8.7	1.61	6.8	149	69	88	156	157
	6.28 p.m.								
Serum 3.	6.09 "	20*		10.0	141	114	18	151	132

* Amount of whole blood.

concentration of sodium in both juice and serum increased in the same manner as in these injections of sodium chloride.

In Table III are tabulated the compositions of pancreatic juice and serum before and after the intraarterial injection of 10 per cent potassium chloride. The injection caused no noticeable effect on the secretion of juice. Before the injection, the sodium and potassium concentration per volume of juice showed the usual excess over the serum values. After the injection there was a

delayed rise in the potassium concentration of the serum with an even smaller rise in the juice. This small rise in the juice might be attributed to the fact that the delayed rise in the serum potassium had not yet made itself evident in the juice samples collected.

TABLE IV.

Injection of Potassium Chloride and Sodium Acid Phosphate.

Dog 24, weight 12.2 kilos.

Sample.	Time.	Amount.	Total solids.	mm per liter.						
				K	Na	PO ₄	HCO ₃	Cl	Na + K	PO ₄ + Cl + HCO ₃
		cc.	gm. per 100 cc.							
Juice 1.	10.40– 11.04 a.m.	7.4	2.87	7.0	160	0.18	119	40	167	159
Serum 1.	11.15 “	30*		4.8	146	3.6	22	106	151	132
Juice 2.	11.04– 11.36 a.m.	5.6	2.09	5.2	162		126	33	167	159
Injection.	11.40– 11.58 a.m.	20	Injection of KCl, 10 per cent intra-arterially.							
Serum 2.	12.08 p.m.	20*		7.3	143	3.4	20	107	150	130
Juice 3.	12.10– 12.32 p.m.	7.2	2.32	10.3	163	0.16	113	52	173	165
“ 4.	12.32– 1.09 p.m.	7.5	1.89	12.2	165	0.13	110	55	177	165
Serum 3.	1.03 “	25*		10.0	137	3.0	19	105	147	127
Injection.	1.07– 1.33 p.m.	30	Injection of NaH ₂ PO ₄ , 20 per cent intravenously.							
Serum 4.	1.36 “	25*		9.9	152	23.1	11	100	162	134
Juice 5.	1.33– 2.28 p.m.	6.4	2.54	13.4	168	2.1	102	65	181	169
Serum 5.	2.35 “	25*		12.4†	141	19.0	12	98	153	129

* Amount of whole blood.

† Potassium value possibly too high because of hemolysis.

The other constituents of both fluids were but little affected by the injection.

In Table IV are given the results of another potassium chloride injection which are similar to those of the previous experiment. The rise in the concentration of potassium in the serum after in-

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jection was again delayed but the rise in the juice appeared earlier and was of the same magnitude as in the serum. Other values were unaffected by the injection.

Table IV also shows the composition of serum and pancreatic juice before and after the intravenous injection of a 20 per cent solution of sodium acid phosphate. Before the injection the concen-

TABLE V.
Injection of Calcium Chloride.

Dog 22, weight 7.2 kilos.

Sample.	Time.	Amount.	Total solids.	mm per liter.						
				Ca	Na	K	Cl	HCO ₃	Na + K + Ca	Cl + HCO ₃
		cc.	gm. per 100 cc.							
Juice 1.	10.33-	11.4	3.15	1.0	158	6.3	51	100	165	151
" 2.	11.04 a.m.	9.5	2.22	0.9	159	4.0	43	111	164	154
Serum 1.	11.50 "	35*		2.4	144	4.3	112	22	151	134
Injection.	12.09-	10		Injection of CaCl ₂ , 10 per cent intravenously.						
Serum 2.	12.21 "	20*		8.6	137	4.4	121	18	150	139
Juice 3.	12.19 -	9.5	2.25	2.1	146	7.4	67	91	156	158
" 4.	1.10 p.m.	10.4	1.88	1.7	153	5.2	65	95	160	160
Serum 3.†	2.53 p.m.	20*		4.7	123		118	13		131
	2.35 "									

* Amount of whole blood.

† Hemolysis.

tration of phosphate in the juice was one-twentieth that of the serum. (The high phosphate content of the normal serum of this animal was probably caused by previous ergosterol feeding experiments.) After injection, though both fluids contained a higher concentration of phosphate, the juice contained one-tenth as much as the serum. The injection of the acid solution also caused the bicarbonate of the serum to be halved with no appreciable

TABLE VI.

Injection of Calcium Chloride, Magnesium Chloride, and Sodium Acid Phosphate.

Dog 18, weight 24 kilos.

Sample.	Time.	Amount.	N	mm per liter.					
				Ca	Mg	PO ₄	HCO ₃	Cl	HCO ₃ + Cl
		cc.	gm. per 100 cc.						
Juice 1.	10.59-	7.2	0.14	1.0	0.3	0.5	99	53	152
	11.29 a.m.								
Serum 1.	11.30 "	15*		2.6	1.1	1.8		110	
Juice 2.	11.30 " -	9.0	0.23	1.0	0.3	0.3	98	53	151
	12.15 p.m.								
Injection.	12.24-	24		Injection of CaCl ₂ , 10 per cent intravenously.					
	12.44 p.m.								
Serum 2.	12.50 "	15*		6.3	0.9	2.0		124	
Juice 3.	12.53-	2.2					75	75	150
	1.04 p.m.								
" 4.	1.04-	6.1		1.7	0.3	0.3	99	57	156
	1.21 p.m.								
" 5.	1.21-	6.5	0.18	1.4	0.2		101	53	154
	1.44 p.m.								
Serum 3.	1.45 "	15*		5.1	1.0	2.7		123	
Juice 6.	3.15-	6.3	0.23	2.3	0.4		85	69	154
	4.18 p.m.								
Serum 4.	4.00 "	15*		4.6	1.3				
Injection.	4.22-	24		Injection of MgCl ₂ , 10 per cent intravenously.					
	4.40 p.m.								
Serum 5.	4.47 "	15*		4.7	8.0				
Juice 7.	4.50-	6.4	0.17	1.2	1.2		106	55	161
	5.09 p.m.								
" 8.	5.09-	8.1	0.20	1.3	1.1	0.4	101	59	160
	5.36 p.m.								
Serum 6.	5.35 "	15*		4.0	5.2			125	
Juice 9.	8.15-	5.6		1.7	1.0	0.6	92	69	161
	8.45 p.m.								
Serum 7.	8.25 "	15*		4.0	4.0	4.0		129	
Injection.	8.45-	80		Injection of NaH ₂ PO ₄ , 20 per cent intravenously.					
	9.37 p.m.								
Serum 8.	9.43 "	15*		3.0	3.7	21.2		117	
Juice 10.	9.49-	4.8		0.9	0.7	2.6	90		
	10.00 p.m.								
" 11.	10.00-	9.1	0.26	0.9	0.7	2.6	88	70	158
	10.35 p.m.								

* Amount of whole blood.

change in the juice bicarbonate, which is in agreement with the results reported in the previous paper.

In Table V are presented the results of an intravenous injection of a 10 per cent calcium chloride solution. Before the injection the calcium content of the juice was about one-half that of the serum. After the injection the calcium concentration of the juice was about one-fourth that of the serum, though the total concentration of calcium in both fluids was markedly increased. There was an unexplainable decrease in the sodium content of the serum after the injection which was also manifested in the juice. Other constituents showed the same relations found in the previous experiments.

In Table VI are given the results of the injection of three different salts: calcium chloride, magnesium chloride, and sodium acid phosphate, into the same animal. The results of the injections of calcium chloride and sodium acid phosphate are similar to those of previous experiments. Before the injection of the 10 per cent magnesium chloride solution the concentration of magnesium in the juice was about one-third that of the serum. After the injection the content of magnesium in both fluids increased, but the concentration in the juice was about one-sixth that in the serum.

It is interesting to note in this experiment the increase in inorganic phosphate of the serum caused by the injections of calcium and magnesium chloride. Since calcium and magnesium form insoluble salts with phosphate, the opposite result might be expected. This same observation has also been made by Salvesen, Hastings, and McIntosh (7).

DISCUSSION.

The inorganic composition of pancreatic juice reported here is similar to that to be reported in a paper by Johnston and Ball (8) for juice obtained from dogs with permanent fistulas. This would seem to indicate that the pancreas was functioning normally in the experiments reported in the present paper, despite the possible unfavorable action of anesthetic, operation, and experimental procedures.

The concentrations of sodium and potassium in pancreatic juice are similar to their concentrations in the serum of the same

animal. Experimental variations in the concentrations of these ions in the serum are reflected quantitatively in the pancreatic juice. Thus it would appear that the pancreatic tissue is freely permeable to the sodium and potassium of the blood serum. On the other hand, calcium, magnesium, and phosphate ions appear to filter through the pancreatic tissue only with difficulty. The concentrations of these ions in pancreatic juice are much lower than in the serum, and large increases in their concentrations in the serum are attended by only slight increases in the juice.

The quantitative composition of pancreatic juice in respect to the cations is similar to that of cerebrospinal fluid and bile. If the blood serum is the immediate source of the cations of all these fluids it would seem that the membranes controlling the composition of these fluids are alike in their free permeability to sodium and potassium and their poor permeability to calcium and magnesium ions.

The low calcium concentration of cerebrospinal fluid as compared to serum has been explained by some workers as due to the fact that only the diffusible calcium of the serum appears in the fluid. If the low calcium content of pancreatic juice is explained in the same manner, then the intravenous injection of calcium chloride, presumably causing a large increase in the diffusible calcium of the serum, should cause a correspondingly large increase in the calcium of the juice. That this does not occur would indicate that low concentrations of calcium in the juice are the result of the slight permeability of pancreatic tissue to this ion.

The total organic matter in any particular juice produced by secretin appears to depend on the previous activity of the gland. If a resting pancreas is stimulated, the juice evoked will contain more organic material than that obtained from a gland that has just previously been actively secreting. This would seem to indicate that the enzymes of the juice are produced independently of the fluid. The decreasing organic content of juice during a prolonged secretion provoked by secretin, might then be attributed to a flushing out of the gland's preformed enzymes at a rate far above the rate of formation. This would agree with Mellanby's (9) view that secretin controls the production of only the alkaline fluid, the enzyme production being controlled possibly by a nervous mechanism.

The organic matter usually has a nitrogen content of 16 per cent, though as stated above, percentages ranging from 11 to 28 have been obtained. These variations are well beyond the experimental error of the micro method. Values as high as 28 per cent would suggest the possibility of the presence of some material such as urea. It is hoped that this peculiarity can be further investigated in the future.

TABLE VII.

Total Inorganic Composition of Juice and Serum of Control Periods.

Dog No.	Sample.	Concentration in mm.			
		Cations:		Anions:	
		Per volume.	Per kilo water.	Per volume.	Per kilo water.
19	Juice.	162	165	158	161
	Serum.	147	160	137	149
20	Juice.	163	166	160	163
	Serum.	145	158	139	151
22	Juice.	165	168	151	154
	Serum.	152	165	136	148
23	Juice.	159	162	157	160
	Serum.	151	164	135	147
24	Juice.	168	171	159	162
	Serum.	155	168	132	144
27	Juice.	155	158	142	145
	Serum.	144	157	130	141

Although freezing point determinations indicate that pancreatic juice and serum have identical osmotic pressures, the total inorganic cation and anion concentration per volume of juice is greater than that of the serum. However, if concentrations are expressed in the accepted manner used by those studying osmotic pressure relations, namely per kilo of water, this apparent discrepancy diminishes. In Table VII are shown the total inorganic cation and anion concentrations of juice and serum calculated per volume and per kilo of water. The water content of juice in these calculations

has been assumed to be 98 per cent (Johnston and Ball (8)) and that of the serum 92 per cent (Kerr (2)). The total cation concentration is the sum of sodium, potassium, calcium, and magnesium. In some cases where calcium and magnesium were not actually determined, average normal values for juice and serum were assumed. Total anions represent the sum of the concentrations of chloride, bicarbonate, and phosphate ions. Here also, in some cases, an average normal value for phosphates in both fluids was assumed. These assumptions can cause but a small error in the total, because of the relatively small figures involved.

It will be seen that, when concentrations for both fluids are expressed per kilo of water, the concentrations of base in the two fluids are in good agreement. The concentrations of acid radicals show wider variations, undoubtedly due, in part at least, to the variation in base bound by protein which is present in unequal concentrations in serum and juice.

It will also be noticed in Table VII that in the juice the excess of inorganic base over inorganic acid radicals is quite variable. The variations run from an excess of 3 to 14 millimols per liter. Some of this variation is most certainly due to experimental error. However, the average excess of base in these six experiments is about 8 millimols per liter. This excess of base cannot be bound by the small amount of protein in the juice if the combining capacity of the juice proteins is similar to that of serum proteins. Either the binding power of juice protein is greater than that of the serum protein or other organic radicals are also present to bind part of this base.

Since the concentration of protein in the serum is greater than in the pancreatic juice, there is a possibility that a Donnan effect would exist. No conclusions can be drawn for the individual ions, for in some cases, chloride and bicarbonate, the concentrations in the two fluids are widely different. However, if the concentrations of total anions per kilo of water in both fluids are considered, then a relation exists that would suggest a possible Donnan equilibrium. The pancreatic juice contains an excess of anions over the serum, of a magnitude similar to that which can be calculated on the basis of the different protein content of the two fluids. If, however the concentration of total cations is now considered in both fluids, it will be seen that there is a relation just the opposite

of that which would be expected if a Donnan equilibrium existed; the total cations are present in greater instead of lesser concentration in the juice than in the serum. Hence no definite conclusions can be drawn with regard to a Donnan effect.

SUMMARY.

1. Pancreatic juice and blood serum have identical osmotic pressures.

2. Concentrations of sodium and potassium expressed per kilo of water are similar in the two fluids. The injection of these ions into the blood stream increases their concentrations in both fluids to the same degree. It is therefore concluded that the pancreatic tissue is freely permeable to sodium and potassium.

3. Calcium, magnesium, and phosphate were found in pancreatic juice in concentrations one-twentieth to one-fourth those in blood serum. The intravenous injection of salts yielding these ions in amounts sufficient to increase greatly their concentrations in the serum caused but little increase in their concentrations in the juice. The conclusion is drawn that the pancreas is but slightly permeable to calcium, magnesium, and phosphate ions.

4. The concentration of total organic matter in the juice appears to depend upon the state of activity of the gland previous to the secretion of the juice.

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